EXHIBIT 3

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April 19, 2022

Regarding: Accusations of data falsification by Dr. Hoau-Yan Wang

To whom it may concern,

I am a trained biochemist and molecular biologist with a Ph.D. from the University of Marburg, Germany. I have over 40 years of experience in academic and industrial organizations including, for example, The Scripps Research Institute, CSL Behring, Bayer HealthCare. My research has focused on the development of therapeutic proteins and has resulted in over 60 publications, and 14 patents (3 pending patent applications).

In the course of my studies, I have conducted hundreds of SDS PAGE gels and Western Blots (WB), for which, in the early years of my carrier and into the mid '90s, I had to cast my own gels. I am therefore very familiar with the intricacies of "home-made" gels. I do not have any relationship with Dr. Wang or Cassava Sciences and I am not involved in his field of research.

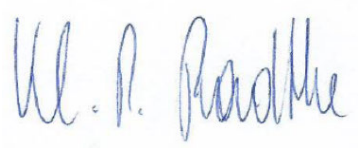
With this letter I am addressing accusations made against Dr. Hoau-Yan Wang (CUNY School of Medicine) alleging fraudulent manipulation of WB data in several publications. These accusations were raised by a Citizen Petition (CP) that was initiated by investors who own short positions on Cassava's stock. In forming these opinions, I analyzed the allegations in the CP, the resulting communication between Dr. Wang and the respective journals, and the original WB data (collectively, "the Materials").

After reviewing the Materials, and conducting my own analysis of the original WBs that were submitted by Dr. Wang, **I conclude that there is absolutely no evidence of fraudulent manipulation of any of the WBs in question**. In fact, as someone who is intimately familiar with the performance of WBs, the allegations against Dr. Wang are surprising and suggest that they are raised by people inexperienced with this methodology. It is also noteworthy that Dr. Wang's publications were accepted in high-impact journals with outstanding reputations. This reputation is a result of a rigorous review process by top experts. Not only were Dr. Wang's papers initially accepted for publication by these journals, but they were also validated in a second review following the CP allegations. The original WBs Dr. Wang provided for this second review confirmed the validity of the data to the editors and reviewing scientist. After reviewing these data myself, I agree.

It is noteworthy that the CP consistently introduces each allegation as a falsification and/or a fabrication of "**clinical trial data**". This is simply not correct. Only one of 8 publications (Publication No. 7) is related to a clinical trial. Knowing that the publications in question relate to an ongoing phase III clinical trial one wonders if using the incorrect term "clinical trial data" is intentional and aimed at confusing Cassava shareholders. Also, the authors of the CP consistently use the wrong term "plot" instead of the correct term "blot." These observations and the unfamiliarity with interpreting WBs creates the impression that the accusing party is not familiar with the subject matter.

Please find my assessment of the individual allegations in Appendix A.

With kind regards,



Peter Radtke, Ph.D.

Appendix A

The CP allegations relate to Western Blot ("WB") images, and mostly fall into three categories:

1) Background features of WBs upon excessive enlargement of printed journal figures, for example lines, different background granulation, and halos around bands, are presented as alleged fraudulent data manipulation.

2) Cropping of background and combining data from different WBs into one figure are alleged as data falsification.

3) The shape and similarities in the appearance of a few different protein bands are alleged as data fabrication or falsification.

Background: The final figure of WBs in a publication is the product of a fairly complex arrangement of many steps that start with sample preparation, casting of the agarose gel, loading of samples, and continue by running the gel by applying an electric current that pulls the proteins into the gel. Subsequently, the gel is dissembled, and the proteins are transferred onto a membrane. In order to minimize unspecific binding the membrane is sequentially incubated with blocking solution a target specific antibody and a labeled antibody-specific antibody that is able to generate chemiluminescence when exposed to a substrate. The membrane is wrapped in clear plastic foil to prevent it from drying and exposed to film within a film cassette. A smaller piece of film is usually cut, to match the size of the blot, and then taped onto a larger piece of exposed film, which acts as support to hold the assembled membrane and film in place within the film cassette. The exposure time determines the intensity of the protein bands and the background. The film is subsequently developed and images of the WBs are arranged and photographed.

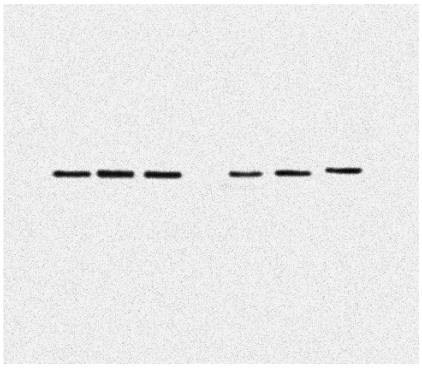
Each of the above steps carries the potential of significantly impacting the appearance of background and bands in the final figure. Also, typically only 10 samples can be run on a gel. Therefore, for experiments that produce more than 10 samples, multiple gels are required and need to be spliced together for the final figure.

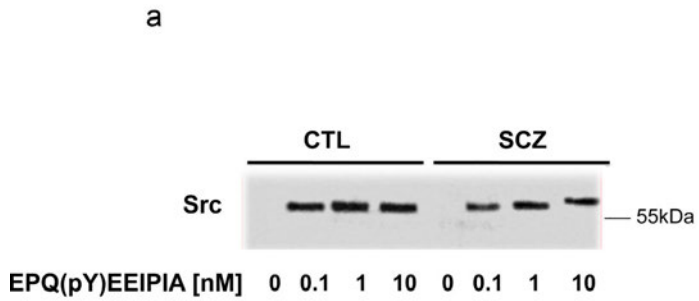
Allegations & Assessment

Allegation 1: Falsification and/or fabrication of WB data and plots of clinical trial data in Figures 4A, S2A and S7 by duplicating, cutting and pasting or altering the plots. Figure 4, Supplementary Figures 2, S3 and S7 are also a concern (1).

Assessment: An "unusually low background noise " in Figure 4 leads to the allegation of potential background removal.

The authors have submitted the original WBs. These originals had been processed for publication in accordance with the *Image Integrity and Standards* of the journal (9) as demonstrated by the submitted originals that clearly show the exact same band pattern, as the published image. An example of an original WB and the respective published figure is shown below. There is no evidence of data falsification.





Original WB in Figure 4a (1) Published image of WB Figure 4a (1)

Allegation 2: Falsification and/or fabrication of WB data and plots of clinical trial data in Figures 4D and 4E (2) by duplicating, cutting and pasting or altering the plots. **Assessment**: The authors have submitted the original WB data. All protein bands in question appear on intact individual blots with continuous background and without any markings that would indicate data manipulation of any kind.

Allegation 3: Falsification and/or fabrication of WB data and plots of clinical trial data in Figures 5A and 6 (3) by duplicating, cutting and pasting or altering the plots. **Assessment:** The cutting and pasting (splicing) of WB results as depicted in Figure 5A is a commonly used and accepted way of visualizing data sets that require more than 10 lanes per gel. It is common practice to run and develop multiple blots under comparable conditions and show the resulting gels/blots side by side within the same figure. In this particular case the data required the showing of 24 lanes. The authors accomplished that by running 3 gels with 8 lanes each and subsequently compiled them into one figure. This is a common, completely acceptable practice and does not amount to fraud. Additionally, Figure 6 shows data derived from a blinded study. The data were unblinded only after the gels/WBs were run. Due to the nature of Figure 6 and the information presented in the context of the publication, as well as the number of samples that were run, the authors had to assemble the relevant bands, in this case the control subject, from different blots, which required cutting and pasting. This method of visualizing data for the reader is acceptable if all blots are run, developed and documented equally without deleting bands. This was done here, and the original WBs provided by the author and the nature of the study demonstrate that no inappropriate data manipulation occurred.

Allegation 4: Falsification and/or fabrication of WB data and plots of clinical trial data in Figures 3 (right panel), 8B, 10A and 12 (4) by duplicating, cutting and pasting or altering the plots. Figure 8B also appears as Figure 3B of R01 AG073350-01 **Assessment:** Figure 3 is alleged to be fabricated due to the presence of a "rectangular box" which appears in the excessively enlarged prints. However, no such rectangular box is seen on the original or enlarged WBs that were provided by the author. A diffuse and darkened background area of unspecific staining, alleged to represent data manipulation, is often seen in WBs. It is likely caused by tape or remnants of glue from tape used to immobilize the blot and film during exposure. Alternatively, contamination of film with glove prints or powder from gloves could also produce such an effect. Figures 8B and C, 10A and B are alleged to be fabricated. However, it is obvious they had to be assembled from different gels due to the limited number of samples that can be run on one gel. The vertical line alleged as indication of inappropriate data manipulation represents the border between adjacent gels that had to

be spliced into one figure due to the limitation of 10-sample per gel. This is an accepted and common practice.

Allegation 5: Falsification and/or fabrication of WB data and plots of clinical trial data in Figure 8A, 8E and 9A (5) by duplicating, cutting and pasting or altering the plots. **Assessment:** The alleged falsifications of data presented in Figures 8A, 8E, and 9A are a simple rearrangement of the original column sequence to match the narrative, graphs and tables presented in the publication with the aim to improved the readability for the reader. The rearrangements were done within the guidelines of the Journal. The original WBs and the rearranged blots were provided by the authors and do not show any irregularities.

Allegation 6: Falsification and/or fabrication of WB data and plots of clinical trial data in in Figure 9A (6) by duplicating, cutting and pasting or altering the plots. **Assessment:** The allegations claim that additional features appear when Figure 9A is altered in Photoshop to reduce brightness and increase contrast. For example, a faint rectangular box, areas with lighter background, and halos around some bands, supposedly represent data falsification by cutting and pasting of bands. As discussed under "Background" there are numerous conditions that can cause these kinds of common artifacts. Some of the most likely causes are tape used to mount the blot and film to a developed film during exposure, sticky glue remnants from tape use in previous exposures, impurities in gels, background from the exposed film used for immobilizing film and blot, shrink wrap that prevents the blot from drying, rollers in the developer, old reagents leading to uneven development of film, contamination from inadvertently touching the film with gloves or powder from gloves, artifacts from reproduction of the original blot, the list goes on. Halos or lighter background intensities observed around bands are not uncommon. There are several possible explanations for their occurrence. In the vicinity of a protein band one does expect a concentration gradient where high protein concentration are found at the center of the band and no protein further away from the band. This concentration difference can be picked up and amplified during the reproduction of the blot. The blot in question demonstrates this phenomenon, as the background granulation around bands changes gradually in a continuum and without disruptions. Noteworthy is the continuum of the background granulation, which indicates authenticity of the bands. Another well know phenomenon that can explain the occurrence of lighter areas (halos) around strong bands is thin-film interference. Thin film interference occurs when light waves reflecting off the top and bottom surfaces of a thin film interfere with one another. If this results in an offset equivalent to half a wavelength it will cause destructive interference, which in turn would result in less bright or lighter areas on the blot. This effect would be most noticeable around the edges of the protein band where gradually lower concentrations of light-producing protein-IgG complexes are found. While it is not possible to determine the exact cause for the observed halos in this particular case, they are a well-known phenomenon.

Allegation 7: Falsification and/or fabrication of WB data and plots of clinical trial data in Figure 3A (7) by duplicating, cutting and pasting or altering the plots 5.7.2 **Assessment:** The allegation states that lanes 8 and 9 in the Plasma pT2310Tau panel have a different background compared to the rest of the blot, alleging data falsification by pasting and cutting. On the original blot provided by the authors it is apparent that the background effects, which start in lane 4 and increase by lane 8 are random, go from top to bottom, across the middle of lanes, and also appear on parts of the gel outside of lane 9. This type of background artifact is so common that it is surprising someone would consider it evidence of data manipulation. It can be caused by different mechanisms but most often it is a result

of high concentrations of unspecific proteins and/or low target protein concentration in the sample. In such cases, lanes have to be "overloaded" with unspecific protein in order to obtain a good signal for the target protein. Here, since the artifact, a vertical streak, goes from top to bottom, and through the center of the bands in lane 8 and 9, it is impossible to come to the conclusion that the data was altered by cutting and pasting. Alternative explanations of the darker background noise in Figure 3A are contamination of photographic equipment, cassettes, rollers and/or development agent, and, as discussed above, tape or glue residue from previously used tapes.

Allegation 8: Falsification and/or fabrication of WB data and plots of clinical trial data in Figures 5B and 10A (8) by duplicating, cutting and pasting or altering the plots.
Assessment: Discontinuities of background granulation in Figure 5B and a sharp dividing line between lanes 2 and 3 that appear with reduced background/contrast in Photoshop are alleged to be indications of data manipulation. However, the gel shown in Figure 5B is a composition of two different experiments, which explains the background difference and the sharp dividing line. Both, blots and images, were generated according to the journal guidelines.
Allegations of background differences in figure 10A and an inconsistent pattern of an additional band can be explained by differences in total protein concentrations of the respective samples. The original blots provided by the author have the same band patterns depicted in the published figure and do not show any signs of manipulation.

References:

1. Banerjee A, Wang HY, Borgmann-Winter KE, MacDonald ML, Kaprielian H, Stucky A, Kvasic J, Egbujo C, Ray R, Talbot K, Hemby SE, Siegel SJ, Arnold SE, Sleiman P, Chang X, Hakonarson H, Gur RE, Hahn CG. Src kinase as a mediator of convergent molecular abnormalities leading to NMDAR hypoactivity in schizophrenia. *Mol Psychiatry* 2015; 20(9):1091-100

2. Talbot K, Wang HY, Kazi H, Han LY, Bakshi KP, Stucky A, Fuino RL, Kawaguchi KR, Samoyedny AJ, Wilson RS, Arvanitakis Z, Schneider JA, Wolf BA, Bennett DA, Trojanowski JQ, Arnold SE. Demonstrated brain insulin resistance in Alzheimer's disease patients is associated with IGF-1 resistance, IRS-1 dysregulation, and cognitive decline. *J Clin Invest.* 2012 Apr; 122(4):1316-38

3. Wang HY, Capuano AW, Khan A, Pei Z, Lee KC, Bennett DA, Ahima RS, Arnold SE, Arvanitakis Z. Insulin and adipokine signaling and their cross-regulation in postmortem human brain. *Neurobiol Aging* 2019; 84:119-130

4. Wang HY, Lee KC, Pei Z, Khan A, Bakshi K, Burns LH. PTI-125 binds and reverses an altered conformation of filamin A to reduce Alzheimer's disease pathogenesis. Neurobiol Aging 2017; 55:99-114

5. Meade GM, Charron LS, Kilburn LW, Pei Z, Wang HY, Robinson S. A model of negative emotional contagion between male-female rat dyads: Effects of voluntary exercise on stress-induced behavior and BDNF-TrkB signaling. Physiol Behav. 2021 May 15; 234:113286

6. Wang S, Li B, Solomon V, Fonteh A, Rapoport SI, Bennett DA, Arvanitakis Z, Chui HC, Miller C, Sullivan PM, Wang HY, Yassine HN. Calcium-dependent cytosolic phospholipase A2 activation is implicated in neuroinflammation and oxidative stress associated with ApoE4. Mol Neurodegener. 2021; 16(1):26

7. Wang HY, Pei Z, Lee KC, Lopez-Brignoni E, Nikolov B, Crowley CA, Marsman MR, Barbier R, Friedmann N, Burns LH. PTI-125 Reduces Biomarkers of Alzheimer's Disease in Patients. J Prev Alzheimers Dis. 2020; 7(4):256-264

8. Stucky A, Bakshi KP, Friedman E, Wang HY. Prenatal Cocaine Exposure Upregulates BDNF-TrkB Signaling. PLoS One 2016 Aug 5; 11(8):e0160585

9. https://www.nature.com/mp/authors-and-referees/editorial-policies#:~:text=Molecular%20Psychiatry%20adheres%20to%20the,for%20important%20intellectual%20content%3B%20and